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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/652,622	08/29/2003	Yawei Ni	04137.0003U3	1025

23859 7590 02/22/2006

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/652,622	NI ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-112 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4,6-39,41-54,56-62,64,68-103 and 105-112 is/are rejected.

7)☒ Claim(s) 5,40,55,63,65-67 and 104 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 29 August 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/14/04; 7/6/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Application is a continuation in part of 09/795,897, now US 6,777,000.

Claims 1-112 are pending and under consideration in this Office Action.

Specification

The first sentence of the specification must be updated to reflect that the priority application 09/795,897 has issued as US Patent 6,777,000.

Clam Objections

Claim 63 is objected to. The word "a" should be substituted for "an".

In claim 91, "phosphste" is misspelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32, 33, 65 and 106-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32 and 33 are indefinite because it is unclear if the solid gel inducing composition phase must be distinct from some other component, or whether it is distinct simply because it is solid. It is also unclear what is intended by "a solid mixture on the molecular level". It is unclear what "on the molecular level" adds to the claim. If

something is solid, it is solid at all levels. Does applicant intend a mixture of individual molecules, rather than e.g. crystals or other particles?

Claim 65 is indefinite because it depends from itself.

Claims 106-110 are indefinite because they are drawn to the "method of claim 91", but claim 91 is drawn to a composition, not to a method.

Claim 111 is indefinite because it recites "the mucosal surfaces" without antecedent basis. It is unclear to which mucosal surfaces the claim is drawn.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 78 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccine comprising a pectic substance as set forth in claim 53, wherein the vaccine increases the amount of IgA specific for the vaccine antigen in lung washings of an animal by about 10% after nasal administration, does not reasonably provide enablement for increasing amounts of IgA specific for any other antigen, or for increasing levels of IgA in lung washings when the composition is not delivered to lung. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 78 is drawn to a vaccine composition that causes an increase in IgA in lung washings of an animal by about 10%. The claim does not limit the nature of the IgA that is increased, or the way in which the composition is administered.

The specification teaches a working example in which mice are administered vaccines intranasally, and anti-vaccine antigen IgA titers increase by greater than 10% in lung washings.

One of skill in the art appreciates that immunoglobulins are by their nature directed against specific antigen three dimensional structures, and would not expect to predictably increase, by administration of a vaccine, the level of IgA against any antigen other than those in the vaccine. Neither would one of skill in the art expect to obtain increased IgA levels in lung washings after intravenous or intramuscular injection of the composition, because the antibodies in lung washings are indicative of a mucosal, not a humoral immune response.

The specification did not teach how to obtain immune responses to antigens other than those in the delivered vaccine, nor how to obtain increased IgA levels in lung washings except by vaccine delivery to lung. As a result one of skill in the art would have to perform undue experimentation in order to use the invention as intended.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 17-24, 27-30, 32-36, and 41-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Degre (US Patent 4,978,528).

Degre taught a solid antibacterial composition comprising dried pectin. See abstract, e.g. claims 10 and 1. The antibacterial composition comprises several compounds, including the proteins lactoperoxidase and lactoferrin, some of which participate in the formation of an antibacterial substance. The pectin functions to separate at least one of the compounds from the others so that the reaction cannot take place until the entire composition is hydrated. After hydration, the reactants can diffuse through the resulting pectin gel and production of the antibacterial substance can occur. The pectin is used to form a calcium-containing gel surrounding one of the reactants by dissolving the pectin and the reactant in an aqueous solution which is then showered in fine calibrated droplets into a solution containing calcium ions, the falling droplets forming pearls of gel of the pectin with the calcium ions, the latter enclosing said substance. Said pearls are collected, dried and then mixed with the other components thereby to form the anti-bacterial composition. See column 3, lines 50-59. The entire antibacterial composition may be in the form of a dry powder. See column 4, lines 38-43. The composition is considered to be a vaccine inasmuch as one would reasonably expect an immune response against the polypeptides comprised in the composition. The composition may also comprise a thickening agent such as carboxymethylcellulose. See sentence bridging columns 4 and 5. The composition may be formulated as a tablet

or capsule. See column 4, lines 55-57. Claim 34 is included in this rejection because the composition comprises physiologically active agents, pectin, and calcium ions present as a physical mixture comprising separate solid components, i.e. some of the physiologically active agents are separate from the pectin and the calcium ions.

Claims 1-4, 6, 17, 18, 22-24, 27-29, 32-36, 41-43, 46, 47, 49, and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Hill (US Patent 3,946,110).

Hill taught methods of making solid, aspirin-containing tablets or powders by mixing together aspirin and a pectin, alginate, or carrageenan. See entire document, especially abstract; paragraph bridging columns 1 and 2; column 2, lines 25-64; Figs. 1-4; column 6, line 59 to column 7, line 35; and column 10, line 37 to column 11, line 18. The compositions can comprise solid calcium salts, see column 2, lines 52-63. The compositions comprise magnesium stearate, which is considered to be a thickener and an excipient. See column 11, lines 5-10. Claim 34 is included in this rejection because the composition comprises physiologically active agents, pectin, and calcium ions present as a physical mixture comprising separate solid components, i.e. some of the physiologically active agents are separate from the pectin and the calcium ions. Claim 34 is included in the rejection because the various components of the composition form powder granules that are themselves separate solid components of the composition. See e.g. Figs 2-4. The formation of a gel is considered to be inherent in the process of oral administration due to the presence of calcium ions in saliva and gastric juices. See column 2, lines 45-55.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 7-16, 53, 54, 56-62, 64, 68, 69, 71-89, 92-100, 102, 103, 105, 111, and 112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Degre (US Patent 4,978,528) in view of Ni et al (US Patent 5,929,051).

Degre taught a solid antibacterial composition comprising dried pectin. See abstract, e.g. claims 10 and 1. The antibacterial composition comprises several compounds, including the proteins lactoperoxidase and lactoferrin, some of which participate in the formation of an antibacterial substance. The pectin functions to separate at least one of the compounds from the others so that the reaction cannot take place until the entire composition is hydrated. After hydration, the reactants can diffuse through the resulting pectin gel and production of the antibacterial substance can occur for controlled release. The pectin is used to form a calcium-containing gel surrounding one of the reactants by dissolving the pectin and the reactant in an aqueous solution which is then showered in fine calibrated droplets into a solution containing calcium ions, the falling droplets forming pearls of gel of the pectin with the calcium ions, the latter enclosing said substance. Said pearls are collected, dried and then mixed with the other components thereby to form the anti-bacterial composition. See column 3, lines

50-59. The entire antibacterial composition may be in the form of a dry powder. See column 4, lines 38-43. The composition is considered to be a vaccine inasmuch as one would reasonably expect an immune response against the polypeptides comprised in the composition. Because the composition has all of the claimed physical characteristics, functional characteristics such as those recited in claim 78 are considered to be inherent. The composition may also comprise a thickening agent such as carboxymethylcellulose. See sentence bridging columns 4 and 5. The composition may be formulated as a tablet or capsule, and may be applied to mucosal surfaces or the eye. See column 4, lines 55-66.

Degre was silent as to the characteristics of the pectin to be used.

Ni taught that a calcium-induced gel-forming aloe pectin (AP 97-1) having a molecular eight of 1.36 X 106 Da, 91% (w/w) galacturonic acid, a degree of methylation of 4.4%, 10.3% (mole/mole) rhamnose, and 0.8% (mole/mole) 3-methoxy rhamnose, was suitable for the controlled release of a physiologically active agent to an animal. See column 5, lines 55-58, Table 10 at columns 19 and 20, column 27, lines 25-67, Figs. 5a-c, and Table 17 at columns 31 and 32. Ni also taught that the pectins were useful for delivering vaccines to mucosal surfaces of animals. See column 5, lines 55-58.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the pectin of Ni in the invention of Degre. One would have been motivated to do so in order to obtain controlled release of the antibacterial substance generated by composition of Degre. Also, MPEP 2144.07 indicates that the selection of

a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). The concentrations of thickener (claim 71), physiologically active agent (claim 79), pectic substance (claims 80-83), and salt (claim 92, would be optimized as a matter of routine, and are obvious absent evidence of unexpected results.

Claims 25, 26, 90, and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Degre (US Patent 4,978,528) and Ni et al (US Patent 5,929,051) as applied to claims 1, 7-16, 53-54, 56-62, 64, 68, 69, 71-73, 79-89, 92-100, and 112 above, and further in view of Gordon et al (US Patent 2,629,665).

The teachings of Degre and Ni are summarized above. These references taught the use of calcium chloride to induce pectin-gel formation, but did not teach the use of calcium phosphate.

Gordon taught that almost any calcium ion, including calcium chloride, mono-calcium phosphate, di-calcium phosphate, etc could be used to cause pectin to form a gel. See column 4, lines 6-15.

It would have been obvious to one of ordinary skill in the art to use calcium phosphate in the invention of Degre, as modified by Ni. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process

for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). In this case, it was well known in the art calcium phosphate could be substituted for the calcium chloride of Degre or Ni. Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness.

Claims 31 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Degre (US Patent 4,978,528) and Ni et al (US Patent 5,929,051) as applied to claims 1, 7-16, 53-54, 56-62, 64, 68, 69, 71-73, 79-89, 92-100, and 112 above, and further in view of Hirabayashi et al (US Patent 5,436,225).

The teachings of Degre and Ni are summarized above. These references taught a powdered composition comprising carboxymethylcellulose as a thickener, but did not teach the use of polyvinylpyrrolidone as a thickener.

Hirabayashi taught that carboxymethylcellulose and polyvinylpyrrolidone could be used as alternative thickeners for powdered compositions.

MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). As a result it would have been obvious to substitute polyvinylpyrrolidone for carboxymethylcellulose in the invention of Degre as modified by Ni.

Claims 1, 7-16, 37-39, 53-54, 56-62, 72, 73, 79-89, 92-95, 97-102, and 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hill (US Patent 3,946,110) in view Ni et al (US Patent 5,929,051).

Hill taught methods of making solid, aspirin-containing tablets or powders by mixing together aspirin and a pectin, alginate, or carrageenan. See entire document, especially abstract; paragraph bridging columns 1 and 2; column 2, lines 25-64; Figs. 1-4; column 6, line 59 to column 7, line 35; and column 10, line 37 to column 11, line 18. The compositions can comprise solid calcium salts, see column 2, lines 52-63. The compositions comprise magnesium stearate, which is considered to be a thickener and an excipient. See column 11, lines 5-10. Claim 34 is included in this rejection because the composition comprises physiologically active agents, pectin, and calcium ions present as a physical mixture comprising separate solid components, i.e. some of the physiologically active agents are separate from the pectin and the calcium ions. Claim 34 is included in the rejection because the various components of the composition form powder granules that are themselves separate solid components of the composition. See e.g. Figs 2-4. The formation of a gel is considered to be inherent in the process of oral administration due to the presence of calcium ions in saliva and gastric juices. See column 2, lines 45-55.

Hill was silent as to the characteristics of the pectin to be used

Ni taught that a calcium-induced gel-forming aloe pectin (AP 97-1) having a molecular eight of 1.36 X 106 Da, 91% (w/w) galacturonic acid, a degree of methylation

of 4.4%, 10.3% (mole/mole) rhamnose, and 0.8% (mole/mole) 3-methoxy rhamnose, was suitable for the controlled release of a physiologically active agent to an animal. See column 5, lines 55-58, Table 10 at columns 19 and 20, column 27, lines 25-67, Figs. 5a-c, and Table 17 at columns 31 and 32. Ni also taught that the pectins were useful for delivering vaccines to mucosal surfaces of animals. See column 5, lines 55-58.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the pectin of Ni in the invention of Hill. One would have been motivated to do so in order to obtain controlled release of the aspirin substance generated by composition of Hill. Also, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). The concentrations physiologically active agent (claim 79), pectic substance (claims 80-83), and salt (claim 92), would be optimized as a matter of routine, and are obvious absent evidence of unexpected results. Also, regarding claims 37-39 and 101, it would have been obvious to one of ordinary skill in the art to suspend in an aqueous carrier the solid powder composition of Hill as modified by Ni, to facilitate oral delivery by drinking. This is considered to be a matter of design choice.

Conclusion

No claim is allowed. Claims 5, 40, 55, 63, 65-67, and 104 are objected to as depending from a rejected claim but would be allowable if rewritten in independent form incorporating all of the limitations of the claim(s) from which they depend.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635